

NON-TECHNICAL ABSTRACT

A Phase I Study of Vaccination with Autologous, Irradiated Melanoma Cells Engineered to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor

No consistently effective therapy exists for metastatic melanoma. Interest in the immunotherapy of melanoma has been stimulated by the observation of rare, spontaneous regressions of disease and the increasing evidence that the host can mount an immunologic response against melanoma. We have conducted extensive laboratory studies using a new strategy for inducing anti-tumor immune responses to mouse tumors, including melanoma. By inserting the immunostimulatory gene granulocyte-macrophage colony stimulating factor (GM-CSF) into mouse melanoma tumor cells and injecting them under the skin, systemic anti-tumor immune responses have been induced, resulting in the eradication of implanted tumors at distant sites. Importantly, the tumor vaccine cells could be lethally irradiated after genetic engineering without compromising the efficacy of treatment. We have demonstrated that this retroviral gene transfer system can also be used to introduce the GM-CSF gene into melanoma cells obtained from cancer patients.

This clinical trial will evaluate the safety and toxicities associated with therapeutic vaccinations using autologous melanoma cells engineered to secrete human GM-CSF. Patients will undergo a surgical procedure to obtain melanoma cells for vaccine preparation. The patient cells will be genetically engineered to express the GM-CSF gene and then lethally irradiated. This represents an important safeguard against the introduction into the patient of tumor cells rendered potentially more virulent by laboratory manipulations. Patients will receive injections of the irradiated GM-CSF expressing cells in the skin. Different schedules of vaccination will be tested, ranging from injections every month to every week for a total of three months.

The proposed study seeks to determine the safety and toxicity of administering this type of genetically engineered cancer vaccine. While the study is not intended to assess the efficacy of this treatment, it will provide important information that will be incorporated into future efficacy studies. Measurements will be made in this trial of any immunologic responses stimulated by the vaccine.